Overview

Mitochondrial Disease Working Group: Vision

The National Institute of Neurological Disease and Stroke (NINDS) Mitochondrial Disease (Mito) Vision Common Data Elements (CDEs) Working Group (WG) convened a panel of experts from Europe and the US to create guidelines/CDEs to be used in clinical practice or for research studies. In creating these guidelines, the WG started from already existing CDEs that are broad/general and created new specific CDEs (where indicated) to fill in gaps where there have not been adequate guidelines/CDEs made previously.

During the first teleconference call, the participants proposed other experts in the fields who should be invited to join the Vision WG. When the full WG was finalized, a second teleconference call was organized to discuss the recommendations that would be put together for the initiative. At this teleconference call, Dr. Patrick Yu-Wai-Man was chosen to chair this WG and four separate subworking groups were created: (i) *visual function for different age groups* (made up of Dr. Tony Moore and Dr. Marcela Votruba), (ii) *visual fields* (made up of Dr. Patrick Yu-Wai-Man, Dr. John Keltner and Dr Chris Johnson), (iii) *OCT and fundus imaging* (made up of Dr. Valerio Carelli and Dr. Piero Barboni), and (iv) *visual electrophysiology* (made up of Dr. Graham Holder and Dr. Claire Sheldon). The draft guidelines/CDEs were discussed through emails and at subsequent teleconference calls before the final versions were produced by each subworking group.

The recommendations developed by the Vision WG are generic in nature and applicable to all types of mitochondrial disease. When developing its recommendations, the WG noted that there are different practices worldwide, in particular between North America and Europe, for example, in relation to visual acuity testing in the pediatric population and in visual electrophysiology protocols. Whilst this is not a major problem *per se*, these differences need to be considered carefully when considering the setting up of multicenter studies. There are also some differences between the US Food and Drugs Administration (FDA) and the European Medicines Agency (EMA) with regards to what they would view as being clinically significant changes in terms of visual outcome measures for clinical trials. Although these considerations are beyond the remit of this NINDS initiatives, it highlights the need for a broader discussion between academics and their local regulatory bodies about the need to standardize benchmarks and guidelines.

In summary, this WG recommends that data collection sheets used for a particular study need to be adapted according to the specific aims and objectives, preferably in consultation with an experienced reading center in order to ensure a uniform protocol for data collection across multiple centers. Adequate training of the technicians performing various ophthalmological tests and ongoing quality control is also essential. Several platforms are available for visual field perimetry and optical coherence tomography (OCT) imaging, and which one(s) to use will, to a certain extent, depend on the preference of the investigators and the specific facilities available in their respective study centers. The important point to re-emphasize is to ensure that the same platform and acquisition protocol is used across all the

centers involved to allow for direct comparison and/or grouping of data at the end of the study. For visual electrophysiology, it is imperative that testing is performed to incorporate the ISCEV (International Society for Clinical Electrophysiology of Vision) Standards.